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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LAWRENCE W. COSENZA

Appeal 2010-008654
Application 10/735,203
Technology Center 1600

Before DONALD E. ADAMS, ERIC GRIMES, and STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134(a) involving claims to a therapeutic delivery system and to an organism for delivery of a therapeutic agent. The Patent Examiner rejected the claims as failing to comply with the

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

written description requirement and the enablement requirement. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 1-2, 4, 7-8, 11, and 41 are on appeal. Claim 1 is representative and reads as follows:

1. A therapeutic delivery system for a host comprising:
a therapeutic agent; and
a sacromastigophoric [sic[2]] organism containing said therapeutic agent through packaging and a gene encoding *full length primate Hpr*; said gene further comprising an inducible promoter and encoding a lysosomal targeting sequence.[3]

(Emphasis added to highlight the main dispute.)

The Examiner rejected the claims as follows:

- claims 1-2, 4, 7-8, 11, and 41 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement; and
- claims 1-2, 4, 7-8, 11, and 41 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

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[2] Appellant refers to the organism as sacromastigophoric, but does not define the term. That term does not appear to be used in the art. The art classifies Appellant's preferred organisms, trypanosomes, in the phylum "sarcomastigophora," "a phylum of protozoans that includes forms moving by flagella, pseudopodia, or both and that is divided into the subphyla Mastigophora and Sarcodina." *See e.g.*, www.merriam-webster.com/medical/sarcomastigophora, last visited Nov. 10, 2010.

[3] In response to a restriction requirement, Appellant elected without traverse a therapeutic delivery system comprising a drug or prodrug, the species Trypanosome as the organism, and Hpr as the lytic factor. (*See* Ans. 3; Reply 1.)

WRITTEN DESCRIPTION

The Issue

The Examiner's position is that the Specification does not provide sufficient written description for claim 1's genus "a gene encoding full length primate Hpr protein." (Ans. 5.) The Specification identifies "Hpr" as haptoglobin-related protein, a serum factor said to induce lysis of the parasite *Trypanosoma brucei brucei*. (Spec. 4, ll. 3-16.) The Examiner found that "aside from the human Hpr cDNA sequence and encoded amino acid sequence, the specification does not provide any additional description for any other Hpr genes or proteins from any other primate species." (Ans. 5.) The Examiner found that the primate genus is large, comprising more than 200 species. (*Id.*) However, the Examiner found that at the time of filing "the prior art did not teach a single functional non-human primate Hpr gene." (*Id.*) According to the Examiner, Smith[4] taught that "in non-human primates the only known Hpr gene is found in Chimpanzees, where the gene does not express functional protein due to premature termination of translation." (*Id.*) Further, the Examiner found that neither the Specification nor the prior art taught, suggested, or exemplified the level of sequence and/or structural homology or shared common structures between primate Hpr genes, nor identified a non-human primate species possessing a functional Hpr gene. (*Id.* at 5-6.)

Appellant contends that the disclosure of a complete nucleic acid sequence for human Hpr in its Application "provides sufficient written description of recombinant Hpr." (App. Br. 8.) According to Appellant,

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[4] Andrea B. Smith et al., *Killing of Trypanosomes by the Human Haptoglobin-Related Protein*, 268 SCIENCE 284-286 (1995).

"only humans, baboons, and chimpanzees possess full length Hpr [and] these Hpr genes possess high sequence homology." (*Id.* at 9.) Therefore, Appellant asserts that "[t]he description by nucleotide and amino acid sequence of the cDNA for Hpr recites 'structural features common to the members of the genus' given the high homology between the Hpr genes in primates." (*Id.*, quoting *Regents of the Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997)). Additionally, Appellant asserts that the disclosure of the nucleotide and amino acid sequences identifies "features [that] constitute a substantial portion of the genus" which, according to Appellant, has only three members. (*Id.*) Appellant also asserts that "the recitation of the term Hpr is sufficient to describe the Hpr genes expressed in primates." (*Id.* at 10, citing *Bigham v. Godtfredsen*, 857 F.2d 1415, 1417 (Fed. Cir. 1988) ("[t]he generic term halogen comprehends a limited number of species, and ordinarily constitutes a sufficient written description of the common halogen species.")).

The issue with respect to this rejection is whether the Examiner established that a person of ordinary skill in the art would not credit Appellant with possession of a genus of genes encoding full length primate Hpr protein.

Findings of Fact

1. We agree with the Examiner's explicit findings regarding the scope and content of (1) the Specification, and (2) the Smith paper. (*See* Ans. 5-13.)

2. Smith disclosed:

> [t]he haptoglobin-related protein is the product of a gene triplication event that occurred in apes and Old World monkeys early in primate evolution, resulting in the haptoglobin gene,

> the haptoglobin-related gene and the primate haptoglobin gene (20). In humans, a subsequent homologous unequal crossover took place, leaving the original haptoglobin gene and producing the human haptoglobin-related gene, a hybrid of the haptoglobin-related gene and the primate haptoglobin gene. In nonhuman primates, the sequence of the haptoglobin-related protein is known only for chimpanzees, where a frameshift leads to premature termination of translation (20). The absence of intact haptoglobin-related protein in chimpanzees is consistent with their lack of TLF [trypanosome lytic factor] activity and may explain why the primate most related to humans does not have this protective mechanism (19).

(Smith, 285-86.)

Principles of Law

When an Applicant claims a class, the Applicant "must describe that class in order to meet the description requirement of the statute." *In re Lukach*, 442 F.2d 967, 968 (CCPA 1971). "The adequate written description requirement . . . serves 'to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material.'" *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996) (citation omitted).

Analysis

Independent claims 1 and 11 recite "a gene encoding full length primate Hpr" and independent claim 41 recites "a gene encoding primate Hpr." Appellant does not dispute that the primate genus comprises more than 200 species. However, according to Appellant "only humans, baboons, and chimpanzees possess full length Hpr [and] these Hpr genes possess high sequence homology." (App. Br. 9). For support, Appellant refers to the Specification at 34, ll. 16-17, which reads: "[a] clone containing the known

Hpr gene coding sequence (SEQ ID NO. 28) has been generated as shown in Figure 11." Neither this statement, nor Figure 11 evidences that the total number of species with full-length primate Hpr genes is three, as Appellant argues. Further, the Specification does not evidence the alleged "high degree of sequence identity between members of the genus of primate Hpr genes."

The Examiner provided evidence that Appellant's arguments about other primate Hpr proteins are mistaken. Contrary to Appellant's argument, Smith disclosed that the chimpanzee has an Hpr gene, but that the gene does not encode full length Hpr. (Ans. 5; FF-2.) Appellant offers no evidence to support the attorney argument that baboons and chimpanzees possess full length Hpr with high sequence homology to human Hpr. (App. Br. 9.) The Examiner referred particularly to Smith at 285-86, which explicitly stated that "[i]n nonhuman primates, the sequence of the haptoglobin-related protein is known *only* for chimpanzees." (FF-2, emphasis added.) Smith is direct evidence contrary to Appellant's generalized allegations that a person of skill in the art would take the human protein as representative of other primate Hpr proteins. Consequently, we find that the Examiner provided sufficient evidence that a person of ordinary skill in the art would not credit Appellant with possession of the genus "a gene encoding full length primate Hpr" recited in the claims.

ENABLEMENT

The Issue

The Examiner's position is that the Specification does not provide an enabling disclosure for: (1) making and using a Trypanosome (the disclosed representative sacromastigophoric organism) containing a gene or a cDNA

encoding non-human primate Hpr; (2) delivering a drug or prodrug by lysing any species of Trypanosome containing the drug through expression of human Hpr; and (3) packaging a drug or prodrug in a Trypanosome as claimed for use as a drug delivery system. (Ans. 8.) According to the Examiner, based upon the state of the art, the limited guidance in the Specification, and the breadth of the claims, a skilled artisan would need to perform undue experimentation to make and use the claimed therapeutic delivery system. (*Id.* at 9-13.)

Appellant contends that the instant "specification teaches how a gene encoding Hpr is operative to lyse Trypanosomes as claimed in the subject invention." (App. Br. 12.) According to Appellant, the Specification explains that "[t]he inventive organism constitutively expresses TetR that represses expression of the Hpr gene… [and i]ntroduction of the inducer tetracycline removes TetR from the promoter removing the repression and allowing selectively timed expression of the Hpr gene leading to lysis of the organism." (*Id.*) Appellant thus argues that the Examiner's concern with endocytosis is misplaced. (*Id.* at 13-14.)

Addressing the Examiner's concern with the scope of the genus of full length Hpr genes and proteins, Appellant repeats the arguments used to address the written description rejection. (*Id.* at 14-15.) Addressing the Examiner's concern with packaging drugs into trypansomes, Appellant argues that Specification Examples 1-3 are sufficient guidance to practice the invention. (*Id.* at 16-17.)

The issues with respect to this rejection are whether the evidence supports the conclusions that undue experimentation would be required to

(1) make and use a Trypanosome containing a gene encoding a non-human primate Hpr;

(2) deliver a drug or prodrug by lysing any species of Trypanosome containing the drug through expression of human Hpr; and

(3) package a drug or prodrug in a Trypanosome as claimed for use as a drug delivery system.

Additional Findings of Fact

3. Smith disclosed: "[t]he involvement of the haptoglobin-related protein in TLF-mediated lysis is consistent with the observation that only some apes and Old World monkeys have lytic activity in their serum." (Smith 285.)

4. Shimamura[5] stated: "The ability of [*Trypanosoma brucei*] *rhodesiense* to infect humans may be due to reduced endocytosis of [Trypanosome lytic factor-1] and failure to enter the lysosome." (Shimamura 227.)

Principles of Law

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech, Inc. v. Novo Nordisk, A/S,* 108 F.3d 1361, 1365 (Fed. Cir. 1997) (quoting *In re Wright,* 999 F.2d 1557, 1561 (Fed. Cir. 1993)). The Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *Wright* at 1562. "Even if some of the claimed combinations were

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[5] Masako Shimamura et al., *The lysosomal targeting and intracellular metabolism of trypanosome lytic factor by Trypanosoma brucei brucei*, 115 MOLEC. & BIOCHEM. PARASITOLOGY 227-237 (2001).

inoperative, the claims are not necessarily invalid. . . ." *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

Analysis

(1) Making and using a trypanosome containing a gene encoding a non-human primate Hpr.

We have considered the evidence proffered by the Examiner, but do not find that the Examiner met the burden of establishing a reasonable basis to question the enablement provided for the claimed invention. *Wright,* 999 F.2d at 1562. In particular, we do not find that the Examiner has established that a skilled artisan would have had to perform undue experimentation to find and use the gene for lytic Hpr from other primates. Smith confirms that lytic activity is present in some apes and Old World monkeys. (FF-3.) With respect to isolating primate species of Hpr gene other than human Hpr, we agree with Appellant that methods of sequencing genes were well known and well established in the art at the time of filing. (*See* App. Br. 15.) The Examiner has not established that a skilled artisan at the time of the invention would not have been able to apply the knowledge in the art, along with the instant disclosure to similarly identify, isolate and sequence a non-human Hpr gene having the required lytic function. Further, with respect to using the non-human Hpr, as Appellant has explained, the instant Specification provides working examples demonstrating how to prepare a Trypanosome with an inducible gene encoding full length Hpr comprising an inducible promoter and encoding a lysosomal targeting sequence. (*See id.* at 17.) We conclude that the rejection provides insufficient evidence to show that the experimentation needed would be undue.

(2) Delivering a drug or prodrug by lysing any species of Trypanosome containing the drug.

With respect to lysing any species of Trypanosome through expression of Hpr, we agree with Appellant that the Specification provides sufficient guidance by teaching how the expression of a gene encoding Hpr that is under the control of a Tet inducible promoter is operative to lyse Trypanosomes. (*See* App. Br. 12.) We do not share the Examiner's opinion that Shimamura established a reasonable basis to question the enablement for the claimed invention. According to the Examiner, "the prior art is clear that human Hpr is not active as a lytic agent against all species of Trypanosome...." (Ans. 10-11.) Specifically, the Examiner found that Shimamura taught "that *Trypanosoma brucei rhodensiense* [sic] is not lysed by Hpr or the TLF [Trypanosome lytic factor] complex comprising Hpr." (*Id.* at 11.) However, we agree with Appellant that Shimamura explained that the reason that *Trypanosoma brucei rhodesiense* is not lysed by Hpr may be due to the reduced endocytosis of TLF/Hpr. (App. Br. 14; FF-2.) As Appellant explains, the invention does not require endocytosis for lysis, as the Hpr is produced within the Trypanosome itself. (*Id.* at 13.) Put another way, because Shimamura discusses endocytosis of TLF/Hpr, it does not weigh against enablement for Appellant's delivery method that does not involve endocytosis of TLF/Hpr. We conclude that the weight of the evidence concerning lysis is insufficient to support a conclusion of undue experimentation regarding that issue.

(3) Packaging a drug or prodrug.

The Examiner acknowledged that the Specification explained that "[n]on-nucleic acid therapeutic agents are packaged in a sacromastigophoric

organism through electroporation or phagocytosis of liposomally packaged therapeutic agents." (Ans. 12.) The Examiner also acknowledged that the Specification referenced three US Patents "as providing guidance for liposomal packaging processes or electroporation." (*Id.*) However, the Examiner found that "[n]either the Specification nor the prior art teach that drugs, either packaged in a liposome ... or not, can be introduced and stably maintained in a Trypanosome, or subsequently released to a host organism upon lysis of the Trypanosome," and concluded that a skilled artisan would require undue experimentation to make and use the claimed delivery system. (*Id.*) What is missing from the Examiner's case is evidence that a skilled artisan would have required further guidance to incorporate a drug or prodrug, packaged according to prior art methods, into a well-characterized Trypanosome. *See Wright*, 999 F.2d at 1562. We conclude that the weight of the evidence concerning drug packaging is insufficient to support a conclusion of undue experimentation regarding that issue.

In sum, we reverse the enablement rejection because there is insufficient evidence to conclude that the full scope of "a gene encoding full length primate Hpr" is not enabled.

CONCLUSIONS OF LAW

The Examiner established that a person of ordinary skill in the art would not credit Appellant with possession of the claimed invention.

We conclude there is insufficient evidence to support the enablement rejection.

SUMMARY

We affirm the rejection of claims 1-2, 4, 7-8, 11, and 41 under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement.

We reverse the rejection of claims 1-2, 4, 7-8, 11, and 41 under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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